FILE 'HOME' ENTERED AT 18:31:22 ON 02 DEC 1999

=> file registry

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

ENTRY 0.60 SESSION 0.60

FILE 'REGISTRY' ENTERED AT 18:33:48 ON 02 DEC 1999
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STRUCTURE FILE UPDATES: 01 DEC 99 HIGHEST RN 249649-97-6

DICTIONARY FILE UPDATES: 01 DEC 99 HIGHEST RN 249649-97-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

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=> s gatggagggcggcatggcggg/sqsn

L1 249 GATGGAGGGCGGCATGGCGGG/SQSN

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

ENTRY SESSION

24.20 24.80

FILE 'CAPLUS' ENTERED AT 18:36:24 ON 02 DEC 1999
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FILE COVERS 1967 - 2 Dec 1999 VOL 131 ISS 23 FILE LAST UPDATED: 1 Dec 1999 (19991201/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s 11 and adenosine

5 L1 55296 ADENOSINE

584 ADENOSINES 55424 ADENOSINE

(ADENOSINE OR ADENOSINES)

L2

5 L1 AND ADENOSINE

=> d fhitstr ibib abs 1-5

L2 ANSWER 1 OF 5 CAPLUS COPYRIGHT 1999 ACS

IT 186470-20-2

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adenosine Al receptor-specific; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

RN 186470-20-2 CAPLUS

CN DNA, d(P-thio)(G-A-T-G-G-A-G-G-G-C-G-G-C-A-T-G-G-C-G-G) (9CI) (CA INDEX

NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

ACCESSION NUMBER:

1999:219995 CAPLUS

DOCUMENT NUMBER:

130:306599

TITLE:

Antisense oligonucleotides capable of binding to multiple targets and their use in the treatment of

respiratory disease

INVENTOR(S):

Nyce, Jonathan W.

PATENT ASSIGNEE(S):

East Carolina University, USA

SOURCE:

PCT Int. Appl., 120 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT	NO.	KI	ND	DATE			A	PPLI	CATI	ои ис	э.	DATE			
WO 9913	886	 A	1 _	1999	0325)	M ₍	0 19	98-U	s194	 19	1998	0917		
W:	AL, A	м, АТ,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
	DK, E	E, ES,	FI,	GB,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IS,	JP,	KE,	KG,
	KP, K	R, KZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
	NO, N	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,		
	UA, U	G, US,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM	
RW:	GH, G	M, KE,	LS,	MW,	SD,	SZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,	DK,	ES,
	FI, F	R, GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,
	CM, G	A, GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG						
AU 9893	951	A	1	1999	0405		A	J 19	98-93	3951		1998	0917		
PRIORITY APP	LN. IN	FO.:					U	S 19	97-5	9160		1997	0917		
							U	s 19	98-93	3972		1998	0609		
							W	19	98-U	S1941	19	1998	0917		

AB Antisense oligonucleotides carrying sequences that will allow them to bind

to more than one mRNA in a target cell are described. Such oligonucleotides can be used as a single treatment for diseases having more than one contributing pathway. In particular, oligonucleotides effective against genes involved in the etiol. of respiratory disease are targeted. Preferably, the oligonucleotides are low in adenosine (.ltoreq.15%) and may have adenosines substituted with analogs. These oligonucleotides are targeted to high (G+C) sequences within mRNAs.

L2 ANSWER 2 OF 5 CAPLUS COPYRIGHT 1999 ACS

IT 208884-01-9

RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (nucleotide sequence; antisense oligonucleotides for treatment of

respiratory ailments and lung inflammation)

RN 208884-01-9 CAPLUS

CN DNA (synthetic human adenosine Al receptor mRNA-binding cDNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

ACCESSION NUMBER: 1998:385522 CAPLUS

DOCUMENT NUMBER: 129:72195

TITLE: Agent and method of treatment for diseases and

conditions associated with respiratory ailments and

lung inflammation

INVENTOR(S): Nyce, Jonathan W.

PATENT ASSIGNEE(S): East Carolina University, USA; Nyce, Jonathan W.

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

Patent

DOCUMENT TYPE:

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PAT	CENT	NO.		KI	ND :	DATE			A)	PPLI	CATI	ои ис	٥.	DATE			
					:			_									
WO	9823	294		A	1	1998	0604	$\overline{}$	W	0 19	97–ช	S220	17	1997	1126		
	W:	ΑL,	AM,	ΑT,	AU,	AZ,	BA,	ВВ,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
		DK,	EE,	ES,	FΙ,	GB,	GE,	HU,	ID,	IL,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,
		LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,
														UA,			
				ZW,										•	•	•	•
	RW:													DK,	ES,	FI,	FR,
														CG,			-
				MR,					•		•	•	•	•	•	•	•
AU	9853			A.		-			ΑŪ	J 199	98-53	3688		1997	1126		
EP	9462	01		A.	1 :	1999	1006		EI	2 199	97-95	5077	5	1997	1126		
														NL,		MC.	PT.
				LT,				•	•		•	,	,			,	,
PRIORITY	APP	LN.	INFO	.:	•	•			US	199	96-75	57024	1 :	19961	126		
									WC	199	97-US	3220	L7 :	19971	126		

AB An agent comprises <u>anti-sense</u> oligos directed to **adenosine**receptors for alleviation of respiratory ailments and inflammation. The
agent is provided as a compn., various formulations, and kit. The
present

agents may be administered in an anti-bronchoconstriction and/or

anti-inflammation effective amt. to alleviate the bronchoconstriction and inflammation afflicting a subject. Preferred agents contain anti-sense oligonucleotide targeting the adenosine A1, A2a, A2b and/or A3 receptors and bradykinin B2 receptor. The method is useful for treating patients afflicted with asthma and other respiratory problems. Pharmaceutical formulations are also disclosed.

L2 ANSWER 3 OF 5 CAPLUS COPYRIGHT 1999 ACS

ΙT 188704-72-5

> RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (DNA antisense therapy for asthma in animal model)

RN 188704-72-5 CAPLUS

DNA, d(G-A-T-G-G-A-G-G-C-G-G-C-A-T-G-G-C-G-G-G) (9CI) (CA INDEX NAME) CN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

1997:145753 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 126:246517

TITLE:

SOURCE:

DNA antisense therapy for asthma in an animal model

AUTHOR(S): Nyce, Jonathan W.; Metzger, W. James Dep. Molecular Pharmacology, EpiGenesis, Pharmaceuticals, Greenville, NC, 27834, USA Nature (London) (1997), 385 (6618), 721-725 CODEN: NATUAS; ISSN: 0028-0836 CORPORATE SOURCE:

PUBLISHER: Macmillan Magazines

DOCUMENT TYPE: Journal LANGUAGE: English

Asthma is an inflammatory disease characterized by bronchial hyper-responsiveness that can proceed to life-threatening airway obstruction. It is one of the most common diseases in industrialized countries, and in the United States accounts for about 1% of all health care costs. Asthma prevalence and mortality have increased dramatically over the past decade, and occupational asthma is predicted to be the pre-eminent occupational lung disease in the next decade. evidence suggests that adenosine, an endogenous purine that is involved in normal physiol. processes, may be an important mediator of bronchial asthma. In contrast to normal individuals, asthmatic individuals respond to adenosine challenge with marked airway obstruction, and concns. of adenosine are elevated in the bronchoalveolar lavage fluid of asthma patients. We performed a randomized crossover study using the dust mite-conditioned allergic

model of human asthma. Administration of an aerosolized phosphorothioate antisense oligodeoxynucleotide targeting the adenosine A1 receptor desensitized the animals to subsequent challenge with either adenosine or dust-mite allergen.

L2 ANSWER 4 OF 5 CAPLUS COPYRIGHT 1999 ACS

TΤ 186470-20-2P

RL: BAC (Biological activity or effector, except adverse); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); USES (Uses) (method of treatment for lung diseases using antisense oligonucleotides)

RN186470-20-2 CAPLUS

CN DNA, d(P-thio)(G-A-T-G-G-A-G-G-G-C-G-C-A-T-G-G-C-G-G-G) (9CI) INDEX

NAME)

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*** STRUCTURE DIAGRAM IS NOT AVAILABLE
ACCESSION NUMBER:
                         1997:145207 CAPLUS
DOCUMENT NUMBER:
                          126:148487
TITLE:
                         Method of treatment for lung diseases using antisense
                          oligonucleotides
                         Nyce, Jonathan W.; Metzger, W. James
INVENTOR(S):
                         East Carolina University, USA; Nyce, Jonathan W.;
PATENT ASSIGNEE(S):
                         Metzger, W. James
                         PCT Int. Appl., 71PP
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                      KIND
                             DATE
                                            APPLICATION NO.
                                                             DATE
     WO 9640162
                       Α1
                            19961219
                                           WO 1996-US9306
                                                             19960606
         W: AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE,
             DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG,
             KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
             NZ, PL
         RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
             IE, IT, LU, MC, NL, PT, SE
     US 5994315
                            19991130
                                            US 1995-474497
                                                             19950607
                       Α
    CA 2223776
                       AA
                            19961219
                                            CA 1996-2223776
                                                             19960606
    (AU 9660959)
                                           AU 1996-60959
                       Α1
                            19961230
                                                             19960606
     EP 831848
                            19980401
                                           EP 1996-918260
                                                             19960606
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             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
                                            CN 1996-196115
                                                             19960606
     CN 1192686
                            19980909
     JP 11507218
                       Т2
                            19990629
                                            JP 1996-501658
                                                             19960606
PRIORITY APPLN. INFO.:
                                            US 1995-474497
                                                             19950607
                                            WO 1996-US9306
                                                             19960606
     A method of treating airway disease in a subject in need of such
treatment
     is disclosed. The method comprises topically administering to the
subject
     an antisense oligonucleotide in an amt. effective to treat the airway
     disease, where the antisense oligonucleotide is essentially free of
     adenosine. Pharmaceutical formulations are also disclosed.
     ANSWER 5 OF 5 CAPLUS COPYRIGHT 1999 ACS
L2
TΤ
     186470-20-2P
     RL: BAC (Biological activity or effector, except adverse); BPR
(Biological
     process); PNU (Preparation, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (antisense oligonucleotides directed against adenosine Al or
        A3 receptors for treatment of asthma)
     186470-20-2 CAPLUS
RN
     DNA, d(P-thio)(G-A-T-G-G-A-G-G-G-C-G-G-C-A-T-G-G-C-G-G-G) (9CI)
CN
INDEX
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
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1997:130067 CAPLUS

ACCESSION NUMBER:

DOCUMENT NUMBER: TITLE: INVENTOR(S): PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE: PATENT NO. WO 96402667

126:135600

Antisense oligonucleotides directed against

APPLICATION NO.

US 1995-472527

AU 1996-60295

WO 1996-US8325

DATE

19950607

19960603

19960603

adenosine A1 or A3 receptors for treatment of

asthma

Nyce, Jonathan W.

East Carolina University, USA; Nyce, Jonathan W.

PCT Int. Appl., 34 pp.

CODEN: PIXXD2

Patent

English

KIND DATE

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

_____ Α1 19961219 WO 1996-US8325 19960603 AL, AM, AT, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE CA 2223769 AΑ 19961219 CA 1996-2223769 19960603 AU 9660295 A1 19961230 AU 1996-60295 19960603 AU 699330 В2 19981203 EP 831924 A1 19980401 EP 1996-917910 19960603 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI CN 1192158 Α 19980902 CN 1996-195955 19960603 AU 9918574 Α1 19990506 AU 1999-18574 19990303

A method of reducing bronchoconstriction in a subject in need of such treatment is disclosed. The method comprises administering to the subject

an antisense oligonucleotide mol. directed against the A1 or A3 adenosine receptor in an amt. effective to reduce

bronchoconstriction. The method is useful for treating patients afflicted

with asthma. Pharmaceutical formulations are also disclosed.

=> d fhitstr 1-5

PRIORITY APPLN. INFO.:

L2 ANSWER 1 OF 5 CAPLUS COPYRIGHT 1999 ACS

IT 186470-20-2

> RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(adenosine Al receptor-specific; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

RN 186470-20-2 CAPLUS

CN DNA, d(P-thio)(G-A-T-G-G-A-G-G-G-C-G-G-C-A-T-G-G-C-G-G-G) (9CI) INDEX

NAME)

^{***} STRUCTURE DIAGRAM IS NOT AVAILABLE

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ANSWER 2 OF 5 CAPLUS COPYRIGHT 1999 ACS
1.2
IT
     208884-01-9
     RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use);
     BIOL (Biological study); PROC (Process); USES (Uses)
        (nucleotide sequence; antisense oligonucleotides for treatment of
        respiratory ailments and lung inflammation)
RN
     208884-01-9 CAPLUS
CN
     DNA (synthetic human adenosine Al receptor mRNA-binding cDNA) (9CI) (CA
     INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
L2
     ANSWER 3 OF 5 CAPLUS COPYRIGHT 1999 ACS
     188704-72-5
ΤT
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (DNA antisense therapy for asthma in animal model)
RN
     188704-72-5 CAPLUS
CN
     DNA, d(G-A-T-G-G-A-G-G-G-C-G-G-C-A-T-G-G-C-G-G-G) (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
     ANSWER 4 OF 5 CAPLUS COPYRIGHT 1999 ACS
L2
ΙT
     186470-20-2P
     RL: BAC (Biological activity or effector, except adverse); PNU
     (Preparation, unclassified); PRP (Properties); THU (Therapeutic use);
BIOL
     (Biological study); PREP (Preparation); USES (Uses)
        (method of treatment for lung diseases using antisense
        oligonucleotides)
RN
     186470-20-2 CAPLUS
     DNA, d(P-thio)(G-A-T-G-G-A-G-G-G-C-G-G-C-A-T-G-G-C-G-G) (9CI)
CN
                                                                       (CA
INDEX
     NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
L2
     ANSWER 5 OF 5 CAPLUS COPYRIGHT 1999 ACS
ΙT
     186470-20-2P
     RL: BAC (Biological activity or effector, except adverse); BPR
(Biological
     process); PNU (Preparation, unclassified); PRP (Properties); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (antisense oligonucleotides directed against adenosine A1 or
       A3 receptors for treatment of asthma)
     186470-20-2 CAPLUS
     DNA, d(P-thio)(G-A-T-G-G-A-G-G-G-C-G-C-A-T-G-G-C-G-G) (9CI)
                                                                       (CA
CN
INDEX
     NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE
=> d cost
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COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

CONNECT CHARGES SEARCH CHARGES DISPLAY CHARGES	1.33	2.70 24.33 12.25
CAPLUS FEE (5%)		39.28 0.72
FULL ESTIMATED COST	15.20	40.00
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) CA SUBSCRIBER PRICE IN FILE 'CAPLUS' AT 18:38:18 ON 02 DEC 1999	ENTRY	TOTAL SESSION -2.68
=> file registry		
COST IN U.S. DOLLARS FULL ESTIMATED COST	SINCE FILE ENTRY 15.52	SESSION
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

ENTRY

-2.68

SESSION

-2.68

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STRUCTURE FILE UPDATES: 01 DEC 99 HIGHEST RN 249649-97-6 DICTIONARY FILE UPDATES: 01 DEC 99 HIGHEST RN 249649-97-6

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

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POTENTIAL STEREO BOND SEARCH PROBLEM WITH STN EXPRESS WITH DISCOVER! 5.0 (Windows Only) SEE NEWS 9 FOR DETAILS

=> s gttgttgggcatcttgcc/sqsn

CA SUBSCRIBER PRICE

L3 4 GTTGTTGGGCATCTTGCC/SQSN

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	23.60	63.92
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY 0.00	SESSION -2.68

FILE 'CAPLUS' ENTERED AT 18:39:34 ON 02 DEC 1999
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FILE COVERS 1967 - 2 Dec 1999 VOL 131 ISS 23 FILE LAST UPDATED: 1 Dec 1999 (19991201/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> s 13 and antisense

3 L3

14550 ANTISENSE

18 ANTISENSES

14551 ANTISENSE

(ANTISENSE OR ANTISENSES)

L4 3 L3 AND ANTISENSE

=> d fhitstr 1-3

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 1999 ACS

IT 186470-21-3

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (adenosine A3 receptor-specific; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

RN 186470-21-3 CAPLUS

CN DNA, d(P-thio)(G-T-T-G-T-T-G-G-G-C-A-T-C-T-T-G-C-C) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 1999 ACS

IT 186470-21-3P

RL: PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (method of treatment for lung diseases using antisense oligonucleotides)

RN 186470-21-3 CAPLUS

CN DNA, d(P-thio)(G-T-T-G-T-T-G-G-G-C-A-T-C-T-T-G-C-C) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 1999 ACS

IT 186470-21-3P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological

process); PNU (Preparation, unclassified); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC
(Process); USES (Uses)

(antisense oligonucleotides directed against adenosine A1 or A3 receptors for treatment of asthma)

RN 186470-21-3 CAPLUS

CN DNA, d(P-thio)(G-T-T-G-T-T-G-G-G-C-A-T-C-T-T-G-C-C) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

=> d ibib abs 1-3

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 1999 ACS ACCESSION NUMBER: 1999:219995 CAPLUS

DOCUMENT NUMBER:

130:306599

TITLE:

Antisense oligonucleotides capable of

binding to multiple targets and their use in the

treatment of respiratory disease

INVENTOR(S):

Nyce, Jonathan W.

PATENT ASSIGNEE(S):

East Carolina University, USA

PCT Int. Appl., 120 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

SOURCE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

P.A	TENT	NO.		KI	ND	DATE			A	PPLI	CATI	ON NO	э.	DATE			
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		KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	
		NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,
		UG,	US,	UZ,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM	
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		FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,
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PRIORIT	Y APP	LN.	INFO	. :					U	S 19	97-5	9160		1997	0917		
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									W	0 199	98-U	S194	19	1998	0917		

Antisense oligonucleotides carrying sequences that will allow them to bind to more than one mRNA in a target cell are described. Such oligonucleotides can be used as a single treatment for diseases having more than one contributing pathway. In particular, oligonucleotides effective against genes involved in the etiol. of respiratory disease are targeted. Preferably, the oligonucleotides are low in adenosine (.ltoreq.15%) and may have adenosines substituted with analogs. These oligonucleotides are targeted to high (G+C) sequences within mRNAs.

Thus,

in protection against aeroallergen-induced bronchoconstriction (house dust

mite), has an unexpected long-term duration of effect (8.3 days for both PC50 adenosine and resistance), and is free of side effects that might be toxic to the recipient. Such oligonucleotides may be used for treating a disease or condition assocd. with lung airway, such as bronchoconstriction, inflammation, or allergies.

ANSWER 2 OF 3 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER:

1997:145207 CAPLUS

DOCUMENT NUMBER:

126:148487

TITLE:

Method of treatment for lung diseases using

antisense oligonucleotides

INVENTOR(S):

Nyce, Jonathan W.; Metzger, W. James

PATENT ASSIGNEE(S):

East Carolina University, USA; Nyce, Jonathan W.;

Metzger, W. James

SOURCE:

PCT Int. Appl., 71PP CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:



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PATENT NO.
                      KIND DATE
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                                                             DATE
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                            _____
     WO 9640162 /-
                       A1
                            19961219
                                           WO 1996-US9306
                                                             19960606
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             KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
             NZ, PL
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             IE, IT, LU, MC, NL, PT, SE
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                            19991130
                                           US 1995-474497
                                                             19950607
     CA 2223776
                            19961219
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                            19961230
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                                                             19960606
     EP 831848
                       A1
                            19980401
                                           EP 1996-918260
                                                             19960606
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             IE, FI
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                            19980909
                       Α
                                           CN 1996-196115
                                                             19960606
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                       Т2
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                                           JP 1996-501658
                                                             19960606
PRIORITY APPLN. INFO.:
                                           US 1995-474497
                                                             19950607
                                           WO 1996-US9306
                                                             19960606
```

A method of treating airway disease in a subject in need of such treatment

is disclosed. The method comprises topically administering to the subject

an antisense oligonucleotide in an amt. effective to treat the airway disease, where the antisense oligonucleotide is essentially free of adenosine. Pharmaceutical formulations are also disclosed.

ANSWER 3 OF 3 CAPLUS COPYRIGHT 1999 ACS

ACCESSION NUMBER:

1997:130067 CAPLUS

DOCUMENT NUMBER:

INVENTOR(S):

126:135600

TITLE:

Antisense oligonucleotides directed against

adenosine A1 or A3 receptors for treatment of asthma

Nyce, Jonathan W.

PATENT ASSIGNEE(S):

East Carolina University, USA; Nyce, Jonathan W.

SOURCE:

PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: .
LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA	rent 1	NO.		KI	ND	DATE			A	PPLI	CATI	ON N	0.	DATE			
	WO	9640	266		A	1	1996	1219		W	0 19	 96-∪	s832	5	1996	0603		
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			DE,	DK,	DK,	EE,	EE,	ES,	FI,	FI,	GB,	GE,	HU,	IL,	IS,	JP,	KE,	KG,
			KP,	KR,	ΚZ,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,	NO,
			ΝZ,	\mathtt{PL}														
		RW:	ΚE,	LS,	MW,	SD,	SZ,	UG,	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,
			ΙE,	IT,	LU,	MC,	NL,	PT,	SE									
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	AU	96602	295		Α	1	1996	1230		Αl	J 19	96-6	0295		1996	0603		
	AU	6993	30		B	2	1998	1203										
	EP	83192	24		Α	1	1998	0401		E	P 19	96-9	1791	0	1996	0603		
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			ΙE,	FI														
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PRIC	DRITY	APP	LN.	INFO	. :					U:	3 19	95-4	7252	7	19950	0607		
										ΑŪ	J 19	96-6	0295		19960	0603		
										W	19	96-U	s832	5	1996	0603		
	-					1							1 .				_	

AB A method of reducing bronchoconstriction in a subject in need of such treatment is disclosed. The method comprises administering to the subject

an **antisense** oligonucleotide mol. directed against the Al or A3 adenosine receptor in an amt. effective to reduce bronchoconstriction. The method is useful for treating patients afflicted with asthma. Pharmaceutical formulations are also disclosed.

=> s gtgggcctagctctcgcc/sqsn

REG1stRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress... Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L6 3 L5

=> d fhitstr 1-3

L6 ANSWER 1 OF 3 CAPLUS COPYRIGHT 1999 ACS

IT 186470-22-4

RN

186470-22-4 CAPLUS

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (adenosine A3 receptor-specific; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

DNA, d(P-thio)(G-T-G-G-G-C-C-T-A-G-C-T-C-T-C-G-C-C) (9CI) (CA INDEX NAME) *** STRUCTURE DIAGRAM IS NOT AVAILABLE L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 1999 ACS ΙT 186470-22-4P RL: PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (method of treatment for lung diseases using antisense oligonucleotides) RN186470-22-4 CAPLUS CN DNA, d(P-thio)(G-T-G-G-C-C-T-A-G-C-T-C-T-C-G-C-C) (9CI) (CA INDEX NAME) *** STRUCTURE DIAGRAM IS NOT AVAILABLE L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 1999 ACS 186470-22-4P RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (antisense oligonucleotides directed against adenosine A1 or A3 receptors for treatment of asthma) RN 186470-22-4 CAPLUS DNA, d(P-thio)(G-T-G-G-G-C-C-T-A-G-C-T-C-T-C-G-C-C) (9CI) CN (CA INDEX NAME) *** STRUCTURE DIAGRAM IS NOT AVAILABLE => d ibib abs 1-3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 1999 ACS ACCESSION NUMBER: 1999:219995 CAPLUS DOCUMENT NUMBER: 130:306599 TITLE: Antisense oligonucleotides capable of binding to multiple targets and their use in the treatment of respiratory disease INVENTOR(S): Nyce, Jonathan W. PATENT ASSIGNEE(S): East Carolina University, USA SOURCE: PCT Int. Appl., 120 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English

F	PA?	ENT	NO.		KI	ND	DATE			Α	PPLI	CATI	ON N	٥.	DATE			
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W	VO	9913	8886		Α	1	1999	0325		W	0 19	98-U	S194	19	1998	0917		
		W:	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,	DE,
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			KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
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															MD,			

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

1

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9893951 A1 19990405 AU 1998-93951 19980917

PRIORITY APPLN. INFO: US 1997-59160 19970917

US 1998-93972 19980609

WO 1998-US19419 19980917

AB Antisense oligonucleotides carrying sequences that will allow them to bind

to more than one mRNA in a target cell are described. Such oligonucleotides can be used as a single treatment for diseases having more than one contributing pathway. In particular, oligonucleotides effective against genes involved in the etiol. of respiratory disease are targeted. Preferably, the oligonucleotides are low in adenosine (.ltoreq.15%) and may have adenosines substituted with analogs. These oligonucleotides are targeted to high (G+C) sequences within mRNAs.

Thus,

dust

phosphorothicate antisense oligonucleotide (HAdA1AS, 5'-gatggagggcggcatggcggg-3') designed for the adenosine Al receptor is provided. HAdA1AS significantly and specifically reduces the in vivo response to adenosine challenge in a dose-dependent manner, is effective in protection against aeroallergen-induced bronchoconstriction (house

mite), has an unexpected long-term duration of effect (8.3 days for both PC50 adenosine and resistance), and is free of side effects that might be toxic to the recipient. Such oligonucleotides may be used for treating a disease or condition assocd. With lung airway, such as bronchoconstriction, inflammation, or allergies.

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 1999 ACS ACCESSION NUMBER: 1997:145207 CAPLUS

DOCUMENT NUMBER:

126:148487

TITLE:

Method of treatment for lung diseases using antisense

oligonucleotides

INVENTOR(S):

Nyce, Jonathan W.; Metzger, W. James

PATENT ASSIGNEE(S):

East Carolina University, USA; Nyce, Jonathan W.;

Metzger, W. James PCT Int. Appl., 71PP

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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WO	9640	162		A	1	1996	1219		W	0 19:	 96-∪	 s930	- - 6	1996	 0606		
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CN	1192	686		Α		1998	0909		CI	1 199	96-19	9611	5	19960	0606		

JP 11507218 T2 19990629 JP 1996-PRIORITY APPLN. INFO.: US 1995-

JP 1996-501658 19960606 US 1995-474497 19950607 WO 1996-US9306 19960606

AB A method of treating airway disease in a subject in need of such treatment

is disclosed. The method comprises topically administering to the subject

an antisense oligonucleotide in an amt. effective to treat the airway disease, where the antisense oligonucleotide is essentially free of adenosine. Pharmaceutical formulations are also disclosed.

L6 ANSWER 3 OF 3 CAPLUS COPYRIGHT 1999 ACS ACCESSION NUMBER: 1997:130067 CAPLUS

DOCUMENT NUMBER: 126:135600

TITLE: Antisense oligonucleotides directed against adenosine

Al or A3 receptors for treatment of asthma

INVENTOR(S): Nyce, Jonathan W.

PATENT ASSIGNEE(S): East Carolina University, USA; Nyce, Jonathan W.

SOURCE: PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PA'	TENT	NO.		KI:	ND 	DATE			A	PPLI	CATI	ON N	0.	DATE			
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			NZ,								-	·	•	·	•	•	. •	•
		RW:	KE,	LS,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FI,	FR.	GB,	GR.
							NL,				•	•	·	•		_ •		
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	ΑU	9660	295		A.	1	1996	1230		Αl	J 199	96-6	0295		1996	0603		
	ΑU	6993	30		B	2	1998	1203										
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			ΙE,			•	•	•	,	•	•	•	•	•			,	,
	CN	1192	158		Α		1998	0902		Cì	1 199	96-19	9595	5	19960	0603		
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										ΑU	J 199	96-6	0295		19960	0603		
										WC	199	96-US	58325		19960			
7. F)	-	1		,														

AB A method of reducing bronchoconstriction in a subject in need of such treatment is disclosed. The method comprises administering to the subject

an antisense oligonucleotide mol. directed against the A1 or A3 adenosine receptor in an amt. effective to reduce bronchoconstriction. The method is useful for treating patients afflicted with asthma. Pharmaceutical formulations are also disclosed.

=> s ggcggcctggaaagctgagatggagggcggcatggcgggcacaggctgggc/sqsn

REG1stRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress... Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

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L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 1999 ACS IT 208884-01-9
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RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (human adenosine Al receptor-specific; antisense oligonucleotides capable of binding to multiple targets and their use in treatment of respiratory disease)

RN 208884-01-9 CAPLUS

CN DNA (synthetic human adenosine Al receptor mRNA-binding cDNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

ACCESSION NUMBER: 1999:219995 CAPLUS

DOCUMENT NUMBER: 130:306599

TITLE:

Antisense oligonucleotides capable of binding to multiple targets and their use in the treatment of

respiratory disease Nyce, Jonathan W.

INVENTOR(S):

East Carolina University, USA

SOURCE:

PCT Int. Appl., 120 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT ASSIGNEE(S):

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									_								
WO 9	9913			A.										1998			
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	KP, F NO, N				LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,	MN,	MW,	MX,
		NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,
		UA,	UG,	US,	UZ,	VN,	YU,	ZW,	AM,	ΑZ,	BY,	KG,	KZ,	MD,	RU,	ТJ,	TM
	RW:	GH,	GM,	KΕ,	LS,	MW,	SD,	SZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	DK,	ES,
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		CM,	GΑ,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	ΤG					•	•
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PRIORITY											97-59			19970	917		
									U:	s 199	98-93	3972		19980	0609		
									Wo	199	98-US	31941	L9	19980	917		

AB Antisense oligonucleotides carrying sequences that will allow them to bind

to more than one mRNA in a target cell are described. Such oligonucleotides can be used as a single treatment for diseases having more than one contributing pathway. In particular, oligonucleotides effective against genes involved in the etiol. of respiratory disease are targeted. Preferably, the oligonucleotides are low in adenosine (.ltoreq.15%) and may have adenosines substituted with analogs. These

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dust

mite), has an unexpected long-term duration of effect (8.3 days for both PC50 adenosine and resistance), and is free of side effects that might be toxic to the recipient. Such oligonucleotides may be used for treating a disease or condition assocd. with lung airway, such as bronchoconstriction, inflammation, or allergies.

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1999 ACS

IT 208884-01-9

RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(nucleotide sequence; antisense oligonucleotides for treatment of respiratory ailments and lung inflammation)

RN 208884-01-9 CAPLUS

CN DNA (synthetic human adenosine A1 receptor mRNA-binding cDNA) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE

ACCESSION NUMBER: 1998:385522 CAPLUS

DOCUMENT NUMBER: 129:72195

TITLE: Agent and method of treatment for diseases and

conditions associated with respiratory ailments and

lung inflammation

INVENTOR(S): Nyce, Jonathan W.

PATENT ASSIGNEE(S): East Carolina University, USA; Nyce, Jonathan W.

SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA'	TENT	NO.		KI	ND	DATE			A	PPLI	CATI	ON N	э.	DATE			
WO	9823	 294		A	1	1998	0604		W	0 19	 97 - ℧	S220	 17	1997	 1126		
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		DK,	EE,	ES,	FI,	GB,	GE,	HU,	ID,	IL,	IS,	JP,	ΚE,	KG,	KP,	KR,	KZ,
														MX,			
		PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	ТJ,	TM,	TR,	TT,	UA,	UG,	US,	UZ,
						ΑZ,											
	RW:	GH,	ΚE,	LS,	MW,	SD,	SZ,	ŪĠ,	ZW,	AT,	BE,	CH,	DE,	DK,	ĖS,	FI,	FR,
														CG,			
		GN,	ML,	MR,	NE,	SN,	TD,	TG			-		-	-		-	•
AU	9853	688		A:	1	19980	0622		Αl	J 199	98-5	3688		1997	1126		
EP	9462	01		A.	1	1999:	1006		E	P 199	97-9	5077	5	19971	1126		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
						FI,						-		-	_	•	•
PRIORITY	Y APP	LN.	INFO	. :					US	5 199	96-75	57024	1	19961	1126		
									WC	199	97–ชร	5220	L7 :	19971	1126		

AB An agent comprises anti-sense oligos directed to adenosine receptors for alleviation of respiratory ailments and inflammation. The agent is provided as a compn., various formulations, and kit. The present agents